

REMARKS

In this Amendment, Applicant has cancelled Claim 21 and amended Claims 14 and 19. Claim 14 has been amended to include all the limitations of Claim 1. Therefore, Claims 14 – 20 satisfy the unity of invention requirement and should be examined together with Claims 1 – 13. In addition, Claim 19 has been amended to correct an informality. It is respectfully submitted that no new matter has been introduced by the amended claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

REJECTIONS UNDER 35 U.S.C. § 102:

Claims 1 – 3 have been rejected under 35 U.S.C. § 102 (e) as allegedly being anticipated by Schwartz et al. (US 6,495,721), hereinafter Schwartz.

Applicant traverses the rejection and respectfully submits that the present-claimed invention is not anticipated by the cited reference. More specifically, Schwartz teaches the production of sertraline hydrochloride Form-II, NOT sertraline hydrochloride Form V of the present invention.

In addition, the form in which hydrogen chloride added is not defined in Example-11 of Schwartz, and not a single example uses aqueous HCl in Schwartz. However, according to the present invention, hydrogen chloride is required to be added as an aqueous solution i.e. aqueous HCl – “b) reducing the pH of the solution or the suspension by adding hydrochloric acid in water to form a clear solution”.

Furthermore, according to Schwartz, after adding hydrogen chloride and the temperature rises to about 50°C, solution may not be cleared. However, in instant invention, the mixture is required to make clear after adding hydrogen chloride, if required water is added.

Moreover, in Schwartz, a mixture is required to be stirred for 2 hours at a room temperature after cooling. However, in the present invention, the mixture is not required to be stirred additionally after cooling it to room temperature.

With regard to the Examiner's contention that form-V may be an inherent product in the process disclosed in Example 11 of Schwartz, it is respectfully submitted that under MPEP 2112.IV., the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)

More specifically, Applicant respectfully submits that sertraline hydrochloride Form V is not an intermediately produced in the said process. Applicant draws the attention of Examiner that Schwartz discloses preparation of Sertraline hydrochloride Form-II in an Example 11 of its specification, wherein the process uses sertraline mandelate which comprises to obtain reaction mixture of sertraline mandelate & n-butanol, the mixture was acidified with hydrogen chloride until pH 0, wherein temperature rose to ~50C°. Considering the solubility of sertraline in n-butanol, it seems to the person skilled in art that obtained solution is not cleared. Whereas in instant invention, it is necessary to obtained clear solution after pH is reduced and mixture is heated to reflux temp by adding water if required, which is also reflected in the step (b) of examined Claim 1 of the present invention i.e. **(to form a clear solution)**.

According to Examiner, Schwartz discloses that Form V is converted to Form II sertraline (column 4 lines 27-37). Applicant respectfully submits that sertraline Form II is prepared from Form V of sertraline by the granulation of Form V with small amounts of ethanol or methanol and mixture is stirred for at least period of few hours, up to several days, preferably about two days. Corresponding process has been exemplified in Example 7. The Example 7 of Schwartz clearly shows that transformation for 2 gm of Form V to Form II requires stirring for at least two days with small amount of ethanol (0.5 ml). Thus, according to Schwartz two parameters are playing crucial role for the conversion of Form V to Form II; an amount of solvent (ethanol), which is ¼ of weight of sertraline hydrochloride and stirring for at least two days. Whereas, the Example 11 of Schwartz discloses that amount of solvent used is proportionately higher and such stirring (2 days) is also absent.

Furthermore, regarding Examiner's contention that, in Example-11 of Schwartz, Form V is inherently produced and which is later on converted into Form II, please refer the Examples Nos. 3 and 6 of Schwartz. 1) Example 3 (column 6 lines 40-45) discloses that while stirring sertraline HCl form V in ethanol (20ml) alcoholate of Form VI is produced. 2). In Example 6 (column 7) of Schwartz, sertraline Form V is converted into Form II by suspending Form V in DMF and heated 70°C, solution cooled to room temperature to get the Form II of sertraline HCL.

Thus, the above facts clearly indicate that conversion of sertraline form V **directly** in to sertraline form II is certainly possible provided only if it satisfies the following criteria according to Schwartz:

1. Use of specific solvents such as DMF, Cyclohexanol and acetone (Col. 4, Line 45-46).
2. If alcohol is used as solvent, as mentioned in example 7, use of very less quantity of solvent (suitable for granulation) and long stirring time (2 days).

Since none of these criteria are satisfied by Example 11 as mentioned, it can be concluded that during the process for preparation of form-II, Form V would not be an inherently produced and thus the instant invention is not anticipated by Schwartz.

Furthermore, with regard to Examiner's observation of alleged similarity of the instant claimed process steps and the process steps disclosed in Schwartz suggesting that Form V and Form II sertraline are made together. Applicant respectfully submits that there is no possibility of obtaining mixture due to following reasons:

1. As mentioned above, form-V may not be obtained as an intermediary product in the process mentioned in Example 11.
2. According to the disclosure given in column 5 of Schwartz, a mixture of sertraline hydrochloride Form II and sertraline hydrochloride Form V is prepared by heating ethanolate Form VI at 105°C for 24 hours under vacuum (<10mmHg) (please also refer Example 10) to induce the transformation of ethanolate form VI to Sertraline hydrochloride Form II mixed with Form V. The characteristics peak of Form II as mention in US 6495721 at col. 2 line 54-56 are 13.2 and 14.7 2theta and it is quite evident that the Form V as prepared by the instant invention and the data submitted clearly proves that those peaks are absent. Furthermore, the condition to prepare sertraline hydrochloride ethanolate Form VI is stirring sertraline hydrochloride Form V and ethanol absolute at room temperature for 24 hours, whereas in instant invention reaction mixture is not stirred for 24 hours. after cooling.

The differences in process steps of the present invention and Example 11 of Schwartz as mentioned above along with the explanation clearly indicates that there is no possibility of obtaining mixture of form II & form V.

Therefore, the pending claims are not anticipated by Schwartz and the rejection under 35 U.S.C. § 102 has been overcome. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 103:

Claims 1 – 13 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Schwartz.

Applicant traverses the rejection and respectfully submits that the embodiments of present-claimed invention are not obvious over Schwartz. The significant differences between Schwartz and the present invention have been indicated above. Schwartz discloses the preparation of sertraline hydrochloride form V using sertraline base and not using sertraline mandelate, whereas the present invention provides the process for the preparation of sertraline hydrochloride form V directly from sertraline mandelate.

Moreover, in step b) of Claim 1 in the present invention, the pH is reduced using HCL in water to form a clear solution, whereas in Claims 1, 6 & 7 of Schwartz, HCL is added as a solution of hydrogen chloride (isopropyl alcohol & HCL, acetone & HCL, and n-butanol & HCL) or as a hydrochloride gas. The Examples Nos. 4, 5, & 11 of Schwartz also proves that the process for preparation of sertraline hydrochloride form –II requires either HCL in organic solvent or in gas and not in an aqueous solution. Please note that though the step (a) of the present invention uses solvents but when aqueous HCL is added, the final mixture becomes immediately clear solution; whereas in Schwartz, when the HCL is added in the gas form or in organic solvent the final mixture may not be a clear solution.

Furthermore, in the present invention, it is necessary to obtain clear solution after pH is reduced and mixture is heated to reflux temp by adding water if required, which is also reflected in the step (b) of Claim 1 of the present invention i.e. (to form a clear solution).

Because these different reaction parameters play a critical role and which may lead to different polymorphic forms. Slight modification of such parameter may lead to different polymorphic form. Hence, cited prior does not teach, suggest, or motivate the

person skilled in art to prepare sertraline form V directly from sertraline mandelate and thus can not be considered obvious. In summary, there is no motivation to modify Schwartz. Even if it is modified, it will not render the present claimed invention obvious. One of ordinary skill in the art would not discern the present invention as claimed at the time of its invention.

Therefore, the newly presented claims are not obvious over Schwartz and the rejection under 35 U.S.C. § 103 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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